UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/505,138	08/19/2004	Rango Dietrich	26230	1681

26211 7590 10/20/2010
FISH & RICHARDSON P.C. (NY)
P.O. BOX 1022
MINNEAPOLIS, MN 55440-1022

EXAMINER	
HARTLEY, MICHAEL G	
ART UNIT	PAPER NUMBER
1618	

NOTIFICATION DATE	DELIVERY MODE
10/20/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte RANGO DIETRICH, HARTMUT NEY, and
KLAUS EISTETTER

Appeal 2009-014363[1]
Application 10/505,138
Technology Center 1600

Before ERIC GRIMES, DONALD E. ADAMS, and
FRANCISCO C. PRATS, *Administrative Patent Judges*.

PRATS, *Administrative Patent Judge*.

DECISION ON APPEAL[2]

This appeal under 35 U.S.C. § 134 involves claims to processes for preparing oral dosage forms. The Examiner rejected the claims as containing new matter and for obviousness.

---

[1] Oral argument was heard in this case on October 13, 2010.
[2] The two-month time period for filing an appeal or commencing a civil action, as recited in 37 C.F.R. § 1.304, or for filing a request for rehearing, as recited in 37 C.F.R. § 41.52, begins to run from the "MAIL DATE" (paper delivery mode) or the "NOTIFICATION DATE" (electronic delivery mode) shown on the PTOL-90A cover letter attached to this decision.

We have jurisdiction under 35 U.S.C. § 6(b). We reverse.

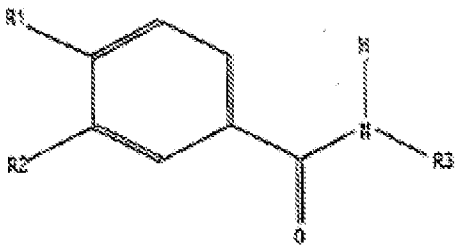
STATEMENT OF THE CASE

"Cyclic nucleotide phosphodiesterase (PDE) inhibitors (specifically of type 4) are currently of special interest as a new generation of active ingredients for treating inflammatory disorders, especially inflammations of the airways such as asthma or airway obstructions" (Spec. 1). However, the low water solubility of some PDE 4 inhibitors, such as the prior art compound roflumilast, "makes it very difficult to produce suitable dosage forms" (*id.*).

The Specification discloses methods for making oral dosage forms "which result[] in rapid, acceptable bioavailability of the PDE 4 inhibitor whose solubility is slight, so as to attain serum levels which are required in order to obtain the desired pharmacological effect quickly without side effects becoming manifest" (*id.* at 2).

Claims 38, 39, 41-48, 53, 54, 65, 68-79, and 81-87 are pending and on appeal (App. Br. 5). Claim 38 is representative and reads as follows:

> 38. A process for producing a dosage form for oral administration of a PDE 4 inhibitor, comprising the steps: (a) producing a mixture of a PDE 4 inhibitor of formula I and one or more pharmaceutical excipients



(I)

in which
R1 is difluoromethoxy,
R2 is cyclopropylmethoxy and
R3 is 3,5-dichloropyrid-4-yl,
or a salt of this compound, an N-oxide of the pyridine of this compound or a salt thereof; and
(b) granulating the mixture obtained in (a) with an aqueous solution of polyvinylpyrrolidone; wherein the dosage form is in tablet or pellet form, wherein said dosage form has immediate release of the PDE 4 inhibitor.

The following rejections are before us for review:

(1) Claims 68 and 82-84, rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement because they contain new matter (Ans. 3-4);

(2) Claims 38, 39, 41, 45-48, 65, 69, 71-79, 81, and 87 rejected under 35 U.S.C. § 103(a) as obvious over Rennard,[3] Ghebre-Sellassie,[4] and Remington[5] (Ans. 4-7);

(3) Claims 68 and 82-84, rejected under 35 U.S.C. § 103(a) as obvious over Rennard, Ghebre-Sellassie, Remington, and Login[6] (Ans. 7-8);

(4) Claims 42-44, 53, 54, 85, and 86, rejected under 35 U.S.C. § 103(a) as obvious over Rennard, Ghebre-Sellassie, Remington, and Chiou[7] (Ans. 9); and

---

[3] U.S. Patent Application Publication 2003/0018071 A1 (published January 23, 2003).
[4] U.S. Patent No. 6,677,362 B1 (issued January 13, 2004).
[5] REMINGTON: THE SCIENCE AND PRACTICE OF PHARMACY, pp. 1618 and 1623-28 (1995).
[6] U.S. Patent No. 5,262,171 (issued November 16, 1993).
[7] Win Loung Chiou and Sidney Riegelman, *Pharmaceutical Applications of Solid Dispersion Systems*, 60 J. PHARM. SCI. 1281-1302 (1971).

(5) Claim 70, rejected under 35 U.S.C. § 103(a) as obvious over Rennard, Ghebre-Sellassie, Remington, and Hatzelmann[8] (Ans. 9-10).

NEW MATTER

ISSUE

The Examiner rejected claims 68 and 82-84 under 35 U.S.C. § 112, first paragraph (Ans. 3-4).

Specifically, the Examiner found that Appellants' insertion of the "'weight average molecular weight' of polyvinylpyrrolidone" into the rejected claims "constitutes new matter" (*id.* at 4). In particular, the Examiner notes, as "shown by the Odian[9] reference, there are at least three different molecular weight averages of polymers: number average, weight average, and viscosity average. Notably, in any particular polymer sample each of these three types of molecular weights has a different vlaue [sic]" (*id.*).

Appellants contend that an ordinary artisan viewing the disclosure of the specific commercial polyvinylpyrrolidone (PVP) products and their corresponding molecular weights on page 7 of the Specification would have understood from the manufacturer's literature that the molecular weights listed for those products corresponded to weight average molecular weights (App. Br. 15). In particular, Appellants note, the weight average molecular

---

[8] Armin Hatzelmann and Christian Schudt, *Anti-Inflammatory and Immunomodulatory Potential of the Novel PDE4 Inhibitor Roflumilast in Vitro*, 297 JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS 267-279 (2001).

[9] George Odian, PRINCIPLES OF POLYMERIZATION, 3d. Ed., pp. 19-23 (1991).

weight ranges disclosed in Beuhler[10] for the various Kollidon products listed on page 7 of the Specification correspond exactly to the molecular weight ranges listed on page 7 (Reply Br. 10). Thus, Appellants argue, an ordinary artisan reading the Specification in light of Beuhler would have recognized that Appellants were in possession of the PVP having the weight average molecular weights recited in the rejected claims (*id.* at 12).

In view of the positions advanced by Appellants and the Examiner, the issue with respect to this rejection is whether the evidence of record supports the Examiner's position that an ordinary artisan viewing the relevant disclosures in the Specification in light of the prior art would have recognized that Appellants were in possession of polyvinylpyrrolidone compositions having the weight average molecular weights recited in claims 68 and 82-84.

FINDINGS OF FACT ("FF")

1. The Specification discloses:

> The polyvinylpyrrolidone (PVP) employed according to the invention is, in particular, a water-soluble PVP with an average molecular weight above 2 000, preferably above 20 000. Examples which may be mentioned are Kollidon 12 PF (molecular weight 2 000-3 000), Kollidon 17 PF (molecular weight 7 000-11 000), Kollidon 25 (molecular weight 28 000-34 000), Kollidon 30 (molecular weight 44 000-54 000), Kollidon 90 F (molecular weight 1 000 000-1 500 000). PVP of higher molecular weight such as, for example, Kollidon 25, Kollidon 30 and Kollidon 90 F may be mentioned as preferred.

(Spec. 7.)

---

[10] Volker Bühler, *Kollidon®, Polyvinylpyrrolidone for the pharmaceutical industry*, 2d. Ed., BASF (1995).

2. The Specification does not state that the molecular weights provided at page 7 are weight average molecular weights.

3. Appellants state, and the Examiner does not dispute, that "Beuhler is a 287 page technical specification published by manufacturer BASF AG for Kollidon® PVP expressly manufactured for, and made commercially available to, the pharmaceutical industry" (Reply Br. 9).

4. Table 17 of Beuhler, reproduced below, shows the weight average molecular weights of each of the Kollidon PVP grades listed on page 7 of Appellants' Specification:

Table 17: Weight and number-averages of the molecular weights of the soluble Kollidon grades

Kollidon grade	Weight-average (recent determinations)	Weight-average (measured before 1975)	Number-average (older determinations)
Kollidon 12 PF	2000 – 3000	2500	1300
Kollidon 17 PF	7000 – 11000	9000	2500
Kollidon 25	28000 – 34000	25000	6000
Kollidon 30	44000 – 54000	40000	12000
Kollidon 90 F	1000000 – 1500000	700000	360000

(Beuhler 36.)

5. As can be seen, the weight average molecular weight ranges for each of the Kollidon grades in Table 17 of Beuhler correspond exactly to the molecular weight ranges of Kollidon grades supplied at page 7 of Appellants' Specification.

PRINCIPLES OF LAW

As stated in *TurboCare Div. of Demag Delaval Turbomachinery Corp. v. General Elec. Co.*, 264 F.3d 1111, 1118 (Fed. Cir. 2001):

> The written description requirement and its corollary, the new matter prohibition of 35 U.S.C. § 132, both serve to ensure that the patent applicant was in full possession of the claimed subject matter on the application filing date. When the applicant adds a claim or otherwise amends his specification after the original filing date . . ., the new claims or other added material must find support in the original specification.

Thus, as the Federal Circuit stated in *Ariad Pharmaceuticals, Inc. v. Eli Lilly and Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010), the "test for sufficiency is whether the disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date."

Beyond simple possession, however, the Federal Circuit also explained that the "test requires an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art. Based on that inquiry, the specification must describe an invention understandable to that skilled artisan and show that the inventor actually invented the invention claimed." *Id.*

ANALYSIS

We agree with Appellants that the Specification, when viewed from the perspective of an ordinary artisan, would have conveyed that Appellants were in possession of, and actually invented, processes using PVP having the weight average molecular weights recited in claims 68 and 82-84.

As Appellants point out, page 7 of the Specification provides a list of PVP products useful in the claimed invention, as well as the molecular weights of those products (FF 1). As Appellants also point out, Beuhler, which is essentially the manufacturer's literature describing those PVP products, discloses that the weight average molecular weights of each of

those PVP products corresponds exactly to the molecular weights provided on page 7 of the Specification (FF 3, 4).

Thus, we agree with Appellants that an ordinary artisan viewing the Specification would have understood from the manufacturer's literature that the molecular weights disclosed on page 7 corresponded to the weight average molecular weights for the PVP products listed.

Turning to the claims at issue, claim 68 recites a process for producing a PDE 4 inhibitor dosage form that contains polyvinylpyrrolidone "selected from the group consisting of polyvinylpyrrolidone of the weight average molecular weight 28,000 - 34,000, polyvinylpyrrolidone of the weight average molecular weight 44,000 - 54,000 and polyvinylpyrrolidone of the weight average molecular weight 1,000,000 - 1,500,000" (App. Br. 34 (Claims Appendix)).

The weight average molecular weight of the first PVP product recited in claim 68 (28,000 to 34,000) corresponds exactly to the molecular weight of the "Kollidon 25" product listed on page 7 of the Specification (*see* FF 1), and also corresponds exactly to weight average molecular weight for Kollidon 25 disclosed by Beuhler (FF 4). Similarly, the weight average molecular weight of the second PVP product of claim 68 (44,000 to 54,000) corresponds exactly to molecular weights provided for Kollidon 30 in Appellants' Specification and in Beuhler.

The third PVP product recited in claim 68 (molecular weight 1 million to 1.5 million) corresponds exactly to the molecular weights provided in both the Specification and Beuhler for Kollidon 90F (FF 1, 4). Thus, as the weight average molecular weights recited in claim 68 correspond exactly to the weight average molecular weights of products described in the

Specification as being useful in the invention, we agree with Appellants that an ordinary artisan would have recognized that Appellants possessed and invented the subject matter recited in claim 68.

Each of claims 82-84 recites a process for producing a PDE 4 inhibitor dosage form that contains "polyvinylpyrrolidone of the weight average molecular weight 1,000,000 - 1,500,000" (App. Br. 36-37 (Claims Appendix)). As noted above, an ordinary artisan would have recognized from Beuhler that Kollidon 90F is a PVP product that has the claimed weight average molecular weight of 1 million to 1.5 million (FF 4). As also noted above, the Specification discloses that Kollidon 90F was a PVP product useful in the claimed invention (FF 1).

In sum, as the weight average molecular weights recited in claims 68 and 82-84 correspond exactly to the weight average molecular weights of products described in the Specification as being useful in the invention, we agree with Appellants that an ordinary artisan would have recognized that Appellants possessed and invented the subject matter recited in the rejected claims. We therefore reverse the Examiner's rejection under 35 U.S.C. 112, first paragraph.

OBVIOUSNESS

ISSUE

The Examiner relies on Rennard in each of the appealed obviousness rejections as disclosing the preparation of an immediate release tablet that contains roflumilast, a PDE 4 inhibitor encompassed by the claims, as well as pharmaceutical excipients (*see* Ans. 4). The Examiner finds that Rennard's methods differ from the claimed methods in that "Rennard does

not teach: (1) the addition of polyvinylpyrrolidone (PVP), and (2) granulation on a fluid bed granulator" (*id.*).

The Examiner nonetheless concludes that an ordinary artisan would have considered it obvious to "use PVP in conjunction with the invention of Rennard, to granulate the PVP in a fluid bed granulator before mixing with an additional excipient, such as magnesium stearate, and tabletting the product" (*id.* at 7). The Examiner reasons that PVP would have been "obvious to use because [Ghebre-Sellassie] teaches the specific advantages of said use, such as increasing bioavailability of poorly soluble drugs. Rolflumilast [sic] is known to be a poorly water soluble drug" (*id.*).

Moreover, the Examiner contends, an ordinary artisan would have considered it obvious to "use a wet granulation process because this process is recognized by the art as suitable for making PVP containing dosage forms, because of the advantages Remmington [sic] describes for fluidized bed granulation, and because Ghebre-Sellassie specifically teaches fluid-bed granulation using a solution (wet granulation)" (*id.*).

Appellants contend that the Examiner failed to make a prima facie case of obviousness because the cited references do not teach or suggest the feature of using an aqueous solution of PVP in the step of granulating the claimed active ingredient (App. Br. 17-19; *see also* Reply Br. 13-15).

Further, Appellants argue, the Chiou reference makes it clear that a solid dispersion of PVP and a drug can only be prepared by the solvent method, which uses an organic solvent to co-solubilize the drug and PVP (App. Br. 22-23). Thus, Appellants urge, Chiou teaches away from practicing the claimed process, because an ordinary artisan would have understood from Chiou that, "even though PVP is understood to be water

soluble, water is not useful for preparing a PVP-drug solid dispersion for water low soluble substances using the solvent methods known in the art or suggested by the combination of cited references" (*id.* at 23; *see also* Reply Br. 18).

In view of the positions advanced by Appellants and the Examiner, the issue with respect to this rejection is whether the evidence of record supports the Examiner's position that an ordinary artisan would have considered it obvious, in view of Rennard, Ghebre-Sellassie, Remington, and Chiou, to granulate a PDE 4 inhibitor of formula I with an aqueous solution of PVP.

FINDINGS OF FACT

Rennard

6. Rennard discloses methods "for preventing or treating a fibrotic disease in a mammal by administering to a patient in need thereof an effective amount of a PDE 4-specific inhibitor" (Rennard [0003]).

7. Rennard discloses that a preferred PDE 4 inhibitor "is cis 4-cyano-4-(3-cyclopentyloxy-4-methoxyphenyl)cyclohexan-1-carboxylic acid (Ariflo®). In addition, the following PDE4 inhibitors may be useful in the practice of this invention: . . . roflumilast (CAS reference No 162401-32-3)" (*id.* at [0015].

8. Rennard discloses that "[w]here the composition is in the form of a tablet, any pharmaceutical carrier routinely used for preparing solid formulations may be used. Examples of such carriers include magnesium stearate, terra alba, talc, gelatin, acacia, stearic acid, starch, lactose and sucrose" (*id.* at [0017]).

9. Rennard discloses the preparation, "by standard means" of immediate release tablets containing the PDE 4 inhibitor Ariflo®, lactose monohydrate, microcrystalline cellulose, sodium starch glycolate, magnesium stearate, and Opadry White (*id.* at [0037]).

10. It is undisputed that the PDE 4 inhibitor roflumilast disclosed in Rennard has relatively low water solubility (*see, e.g.,* Spec. 1 (0.53 mg/L at 21° C)).

Ghebre-Sellassie

11. Ghebre-Sellassie discloses "a novel pharmaceutical solid dispersion and the process for its preparation whereby generally water insoluble drugs are combined with a carrier polymer such as polyvinyl pyrrolidone (PVP) without the need for organic solvents and/or high fusion temperatures" (Ghebre-Sellassie, col. 2, ll. 51-54).

12. Ghebre-Sellassie discloses that its process uses "a vehicle such as polyethylene glycol which reduces the transition temperature and facilitates the molecular interaction between the drug and a polymer such as, polyvinyl pyrrolidone (PVP) by partially solubilizing the drug and/or plasticizing the polymer" (*id.* at col. 2, ll. 56-60).

13. Ghebre-Sellassie discloses:

> The surprising and unexpected results of the present invention is the creation of a solid pharmaceutical dispersion comprised of the aforementioned water insoluble drugs and carriers without the need for using organic solvents, fusion (heat) or both (solvent/heat) which are either lengthy and expensive methods or which limit the types of drugs that can be formulated, i.e. heat labile drugs. Surprisingly, it was discovered that the addition of a plasticizer/solubilizer during the mixing of the two components results in a chemical environment that readily lends itself to dispersion formation.

(*Id.* at col. 3, ll. 58-67.)

14. In Ghebre-Sellassie's methods, the "water insoluble drug of interest is first blended with the [PVP] carrier using any appropriate mixer . . . . The [powder] blend is then transferred to a fluid[] bed granulator" (*id.* at col. 4, ll. 9-14).

15. In the meantime, "a plasticizer such as PEG 400 is dissolved in water with a surfactant such as Tween 80 . . . . Once both ingredients are sufficiently dissolved, the solution is sprayed onto the powder blend in the fluid bed granulator," after which the resulting granulation is fed to a high intensity mixer and ultimately processed for tablet formation (*id.* at col. 4, ll. 14-33).

16. Thus, in Examples I and II of Ghebre-Sellassie, the water insoluble drug romiglizone was mixed with PVP in a blender and the resulting mixture transferred to a fluidized bed granulator, to which an aqueous solution of PEG 400 and Tween 80 was added (*id.* at col. 4, l. 41 through col. 5, l. 30).

Remington

17. Remington discloses that the "most widely used and most general method of tablet preparation is the wet-granulation method. . . . The steps in the wet method are weighing, mixing, granulation, screening the damp mass, drying, dry screening, lubrication and compression" (Remington 1623).

18. Initially, the "active ingredient, diluent and disintegrant are mixed or blended well" to produce a powdered blend (*id.*). Then, "[s]olutions of the binding agent are added to the mixed powders with stirring. The powder mass is wetted with the binding solution until the mass has the consistency of damp snow or brown sugar" (*id.*).

19. Remington discloses that PVP is a binding agent that "can be used as an aqueous or alcoholic solution" (*id.* at 1618).

20. Remington discloses that, in fluid bed granulation methods, the "concept was to spray a granulating solution onto the suspended [powdered drug] particles which then would be dried rapidly in the suspending air. The main benefit from this system is the rapid granulation and drying of a batch" (*id.* at 1625).

Chiou

21. Chiou discloses that "[f]or drugs whose GI absorption is rate limited by dissolution, reduction of the particle size generally increases the rate of absorption and/or total bioavailability" (Chiou 1281).

22. Chiou discloses that particle size reduction can be achieved by a number of techniques including conventional trituration and grinding, as well as the "solvent method" (*id.* at 1281-82).

23. Chiou explains that the solvent method involves "dissolving a physical mixture of two solid components in a common solvent, followed by evaporation of the solvent. This method was used to prepare solid dispersions of β-carotene-polyvinylpyrrolidone, griseofulvin-polyvinylpyrrolidone, sulfathiazole-polyvinylpyrrolidone, [and] steroid-polyvinylpyrrolidone" (*id.* at 1283 (citations omitted)).

24. Chiou discloses, however, that "[d]ue to the chemical stability of polyvinylpyrrolidone to heat and its high melting point . . . the drug-polyvinylpyrrolidone solid dispersions can only be prepared by the solvent method" (*id.* at 1292 (citation omitted)).

PRINCIPLES OF LAW

As stated in *In re Oetiker*, 977 F.2d 1443, 1445 (Fed. Cir. 1992):

> [T]he examiner bears the initial burden . . . of presenting a *prima facie* case of unpatentability. . . .
>
> After evidence or argument is submitted by the applicant in response, patentability is determined on the totality of the record, by a preponderance of evidence with due consideration to persuasiveness of argument.

With respect to establishing obviousness, as the Federal Circuit recently stated, "it is not enough to simply show that the references disclose the claim limitations; in addition, 'it can be important to identify a reason that would have prompted a person of ordinary skill in the art to combine the elements as the new invention does.'" *Transocean Offshore Deepwater Drilling, Inc. v. Maersk Contractors USA, Inc.*, --- F.3d ----, 2010 WL 3257312 at *4 (Fed. Cir. 2010) (quoting *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 401 (2007)).

Ultimately therefore, "[i]n determining whether obviousness is established by combining the teachings of the prior art, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art." *In re GPAC Inc.*, 57 F.3d 1573, 1581 (Fed. Cir. 1995) (internal quotations omitted).

ANALYSIS

We agree with Appellants that the Examiner has not shown, by a preponderance of the evidence, that an ordinary artisan would have considered it obvious, in view of Rennard, Ghebre-Sellassie, Remington, and Chiou, to granulate a PDE 4 inhibitor of formula I with an aqueous solution of PVP.

We acknowledge Remington's disclosure that when PVP is used as a binder in dosage preparation methods involving a granulation step, the PVP

may be added to the drug in the form of an aqueous or alcoholic solution (FF 18, 19). We are not persuaded, however, that Remington's general teaching would have prompted an ordinary artisan to use that technique to granulate a drug of low water solubility, like Rennard's roflumilast.

Specifically, the only cited reference asserted by the Examiner as granulating a drug with low water solubility, like the drug in Appellants' claims, is Ghebre-Sellassie (FF 14). In contrast to the claimed methods, Ghebre-Sellassie mixes the PVP with the drug in dry form, and then granulates the dry-mixed drug/PVP combination in an aqueous solution that contains a PEG plasticizer and a surfactant (*see* FF 14, 16).

We acknowledge, as the Examiner points out, that Ghebre-Sellassie uses the same fluidized bed granulation methods described in Remington as having certain benefits (FF 14, 16, 20). However, the Examiner points to no specific teaching in any of the cited references suggesting that it would have been advantageous, or even useful, to include in Ghebre-Sellassie's aqueous granulation solution any ingredients other than the surfactant and plasticizer specified by the reference. Nor has the Examiner adequately explained why an ordinary artisan, even given Remington's general teachings regarding binders, would have been prompted to include PVP in Ghebre-Sellassie's aqueous granulation solution, when the PVP was already mixed with the drug ingredient in dry form.

We note, as the Examiner argues, that Ghebre-Sellassie discloses that organic solvents were not required in processes involving PVP granulation (FF 11, 13), and that this teaching appears to be contrary to Chiou's disclosure that solid dispersions of water-insoluble drugs with PVP require co-solubilization of the drug and PVP in a compatible organic solvent (FF

24). However, even assuming that an ordinary artisan would have been prompted to apply Ghebre-Sellassie's organic solvent-free techniques to Rennard's roflumilast despite Chiou's advice, Ghebre-Sellassie's methods do not include Appellants' claimed step of adding an aqueous PVP solution to a drug/excipient mixture, as noted above.

To the contrary, the only cited prior art that describes mixing PVP with a water insoluble drug discloses that either an organic solvent is required (Chiou (FF 23, 24)), or that the PVP should be mixed with the drug in dry form, before a plasticizer/surfactant-containing aqueous solution is added (Ghebre-Sellassie (FF 14-16)). Given these teachings, we are not persuaded that Remington's disclosure that binding agents, including PVP, were generally used in drug granulation processes in the form of aqueous solutions, would have prompted an ordinary artisan to granulate roflumilast in an aqueous solution of PVP. Moreover, the Examiner points to no teachings in Login or Hatzelmann that remedy this deficiency of Rennard, Ghebre-Sellassie, Remington, and Chiou.

Thus, as we are not persuaded that the cited references would have prompted an ordinary artisan to granulate roflumilast in an aqueous solution of PVP as required by each of independent claims 38, 47, and 53, we reverse the Examiner's obviousness rejections of those claims, as well as their dependents.

SUMMARY

We reverse the Examiner's new matter rejection of claims 68 and 82-84 under 35 U.S.C. § 112, first paragraph.

We also reverse the Examiner's rejection of claims 38, 39, 41, 45-48, 65, 69, 71-79, 81, and 87 under 35 U.S.C. § 103(a) as obvious over Rennard, Ghebre-Sellassie, and Remington.

We also reverse the Examiner's rejection of claims 68 and 82-84 under 35 U.S.C. § 103(a) as obvious over Rennard, Ghebre-Sellassie, Remington, and Login.

We also reverse the Examiner's rejection of claims 42-44, 53, 54, 85, and 86 under 35 U.S.C. § 103(a) as obvious over Rennard, Ghebre-Sellassie, Remington, and Chiou.

We also reverse the Examiner's rejection of claim 70 under 35 U.S.C. § 103(a) as obvious over Rennard, Ghebre-Sellassie, Remington, and Hatzelmann.

REVERSED

alw

FISH & RICHARDSON P.C. (NY)
P.O. BOX 1022
MINNEAPOLIS, MN 55440-1022